

IN THE SPECIFICATION

Please amend paragraph [0003] of the specification *as published* as follows:

[0003] Part of the description of the present invention is a sequence listing of 1430 pages, consisting of ~~SEQ ID No:~~ SEQ ID NO: 1 through ~~SEQ ID No:~~ SEQ ID NO: 10,540.

Please amend paragraph [0006] of the specification *as published* as follows:

[0006] Further, for patients suffering from acute generalized inflammatory conditions (SIRS) the present invention relates to new possibilities of diagnosis that are obtained from experimentally ~~proofed~~ proved findings in connection with the occurrence of changes in gene activity (transcription and subsequent protein expression).

Please amend paragraph [0023] of the specification *as published* as follows:

[0023] The first explanation for the applicability of microarray technology was obtained through clinical studies on the field of cancer research. Here, expression profiles ~~proofed~~ proved to be valuable with regard to identification of activities of individual genes or groups of genes, correlating with certain clinical phenotypes [17]. Many samples of individuals with or without leukemia or diffuse lymphoma of large B-cells were analyzed and gene expression labels (RNA) were found and used for the classification of those kinds of cancer [17, 18]. Golub et al. found out that an individual gene is not enough to make reliable predictions, however, that predictions made on gene expression profiles of 53 genes (selected from more than 6000 genes that were present on the arrays) are highly accurate [17].

Please amend paragraph [0025] of the specification *as published* as follows:

[0025] To differentiate between symptoms that base on microbial infections and other symptoms of non-infectious etiology, which could indicate sepsis due to their clinical appearance, but are in fact not based on a systemic microbial infection, e.g. of symptoms that base on non-infectious inflammation of individual organs, the determination of gene expression profiles via differential diagnostics ~~proofed~~ proved to be particularly advantageous [19-22]. The use of body fluids for the measurement of gene expression profiles for the diagnosis of SIRS has not yet been described.

Please amend paragraph [0037] of the specification *as published* as follows:

[0037] ~~g)~~ a) Isolation of sample RNA from a sample of a mammal;

Please amend paragraph [0038] of the specification *as published* as follows:

[0038] ~~h)~~ b) Labelling of the sample RNA and/or at least one DNA being a specific gene or gene fragment for sepsis and/or sepsis-like conditions, with a detectable label.

Please amend paragraph [0039] of the specification *as published* as follows:

[0039] ~~i)~~ c) Contacting the sample RNA with the DNA under hybridization conditions;

Please amend paragraph [0040] of the specification *as published* as follows:

[0040] ~~j)~~ d) Contacting sample RNA representing a control for non-pathologic conditions, with at least one DNA, under hybridization conditions, whereby the DNA is a gene or gene fragment specific for sepsis and/or sepsis-like conditions;

Please amend paragraph [0041] of the specification *as published* as follows:

[0041] ~~k)~~ e) Quantitative detection of the label signals of the hybridized sample RNA and control RNA;

Please amend paragraph [0042] of the specification *as published* as follows:

[0042] ~~h)~~ f) Comparing the quantitative data of the marking signals in order to determine whether the genes or gene fragments specific for sepsis and/or sepsis-like conditions are more expressed in the sample than in the control, or less.

Please amend paragraph [0044] of the specification *as published* as follows:

[0044] ~~m)~~ a) Isolation of sample RNA from a sample of a mammal;

Please amend paragraph [0045] of the specification *as published* as follows:

[0045] ~~n)~~ b) Labelling of the sample RNA and/or at least one DNA being a specific gene or gene fragment for severe sepsis, with a detectable label.

Please amend paragraph [0046] of the specification *as published* as follows:

[0046] ~~o)~~ c) Contacting the sample RNA with the DNA under hybridization conditions;

Please amend paragraph [0047] of the specification *as published* as follows:

[0047] ~~p)~~ d) Contacting sample RNA representing a control for non-pathologic conditions, with at least one DNA, under hybridization conditions, whereby the DNA is a gene or gene fragment specific for severe sepsis;

Please amend paragraph [0048] of the specification *as published* as follows:

[0048] ~~g)~~ e) Quantitative detection of the label signals of the hybridized sample RNA and control RNA;

Please amend paragraph [0049] of the specification *as published* as follows:

[0049] ~~h)~~ f) Comparing the quantitative data of the label signals in order to determine whether the genes or gene fragments specific for severe sepsis are more expressed in the sample than in the control, or less.

Please amend paragraph [0057] of the specification *as published* as follows:

[0057] Another embodiment of the invention is characterized in that the gene or gene segment specific for SIRS is selected from the group consisting of ~~SEQ ID No.~~ SEQ ID NO: 6373 to ~~SEQ ID No.~~ SEQ ID NO: 10540, as well as from gene fragments thereof having at least 5-2000, preferably 20-200, more preferably 20-80 nucleotides.

Please amend paragraph [0058] of the specification *as published* as follows:

[0058] Another embodiment of the invention is characterized in that the gene or gene segment specific for sepsis and/or sepsis-like conditions is selected from the group consisting of ~~SEQ ID No.~~ SEQ ID NO: 1 to ~~SEQ ID No.~~ SEQ ID NO: 6242, as well as gene fragments thereof with 5-2000 or more, preferably 20-200, more preferably 20-80 nucleotides.

Please amend paragraph [0059] of the specification *as published* as follows:

[0059] Another embodiment of the invention is characterized in that the gene or gene segment specific for severe sepsis is selected from the group consisting of ~~SEQ ID No.~~ SEQ ID NO: 6243

to ~~SEQ ID No.~~ SEQ ID NO: 6372, as well as gene fragments thereof with 5-2000 or more, preferably 20-200, more preferably 20-80 nucleotides.

Please amend paragraph [0083] of the specification *as published* as follows:

[0083] ~~g)~~ a) Isolation of sample peptides from a sample of a mammal;

Please amend paragraph [0084] of the specification *as published* as follows:

[0084] ~~h)~~ b) ~~Labelling~~ Labeling of the sample peptides with a detectable label;

Please amend paragraph [0085] of the specification *as published* as follows:

[0085] ~~i)~~ c) Contacting the ~~labeled~~ labelled sample peptides with at least one antibody or its binding fragment, whereby the antibody binds a peptide or peptide fragment specific for sepsis and/or sepsis-like conditions;

Please amend paragraph [0086] of the specification *as published* as follows:

[0086] ~~j)~~ d) Contacting the labelled control peptides originating from healthy subjects, with at least one antibody or its binding fragment immobilized on a carrier in form of a microarray, whereby the antibody binds a peptide or peptide fragment specific for sepsis and/or sepsis-like conditions;

Please amend paragraph [0087] of the specification *as published* as follows:

[0087] ~~k)~~ e) Quantitative detection of the label signals of the sample peptides and the control peptides;

Please amend paragraph [0088] of the specification *as published* as follows:

[0088] ~~h)~~ f) Comparing the quantitative data of the label signals in order to determine whether the genes or gene fragments specific for sepsis and/or sepsis-like conditions are more expressed in the sample than in the control, or less.

Please amend paragraph [0090] of the specification *as published* as follows:

[0090] ~~m)~~ a) Isolation of sample peptides from a sample of a mammal;

Please amend paragraph [0091] of the specification *as published* as follows:

[0091] ~~n)~~ b) Labelling of the sample peptides with a detectable label;

Please amend paragraph [0092] of the specification *as published* as follows:

[0092] ~~o)~~ c) Contacting the labelled sample peptides with at least one antibody or its binding fragment, whereby the antibody binds a peptide or peptide fragment specific for severe sepsis;

Please amend paragraph [0093] of the specification *as published* as follows:

[0093] ~~p)~~ d) Contacting the labelled control peptides stemming from healthy subjects, with at least one antibody or its binding fragment immobilized on a carrier in form of a microarray, whereby the antibody binds a peptide or peptide fragment specific for severe sepsis;

Please amend paragraph [0094] of the specification *as published* as follows:

[0094] ~~g)~~ e) Quantitative detection of the label signals of the sample peptides and the control peptides;

Please amend paragraph [0095] of the specification *as published* as follows:

[0095] ~~h)~~ f) Comparing the quantitative data of the label signals in order to determine whether the genes or gene fragments specific for severe sepsis are more expressed in the sample than in the control, or less.

Please amend paragraph [00102] of the specification *as published* as follows:

[0102] Another embodiment of the invention is characterized in that the peptide specific for SIRS is an expression product of a gene or gene fragment selected from the group consisting of ~~SEQ-ID No.~~ SEQ ID NO: 6373 to ~~SEQ-ID No.~~ SEQ ID NO: 10540, as well as gene fragments thereof with 5-2000 or more, preferably 20-200, more preferably 20-80 nucleotides.

Please amend paragraph [00103] of the specification *as published* as follows:

[0103] Another embodiment of the invention is characterized in that the peptide specific for sepsis and/or sepsis-like conditions is an expression product of a gene or gene fragment selected from the group consisting of ~~SEQ-ID No.~~ SEQ ID NO: 1 to ~~SEQ-ID No.~~ SEQ ID NO: 6242, as well as gene fragments thereof with 5-2000 nucleotides or more, preferably 20-200, more preferable 20-80 nucleotides.

Please amend paragraph [00104] of the specification *as published* as follows:

[0104] Another embodiment of the invention is characterized in that the peptide specific for severe sepsis is an expression product of a gene or gene fragment selected from the group consisting of ~~SEQ ID No.~~ SEQ ID NO: 6243 to ~~SEQ ID No.~~ SEQ ID NO: 6372, as well as gene fragments thereof with 5-2000 or more, preferably 20-200, more preferably 20-80 nucleotides.

Please amend paragraph [00145] of the specification (including Table 2) *as published* as follows:

[0145] Table 2 shows that 57 genes of the patient sample were found, which were significantly overexpressed, if compared with the control sample. Table 3 shows that 16 genes of the patient sample were found, which were significantly underexpressed, if compared with the control sample. Those results show that the genes listed in table 2 and table 3 correlate with the occurrence of SIRS. Thus, the gene activities of the genes mentioned are labels for a diagnosis of SIRS.

Table 2: Significantly increased transcription activities and their relative ratio to the control sample in SIRS

GenBank Accession-No.	Hugo-Name	Patient 1	Patient 2	Patient 3	Patient 4	SEQUENCE- ID <u>SEQ ID NO:</u>
XM_051958	ALOX5	2.43	1.49	1.81	1.40	6408
XM_015396	ALOX5AP	3.71	7.39	3.89	2.68	6409
XM_008738	BCL2	1.16	6.76	1.55	1.04	6410
BC016281	BCL2A1	13.71	10.29	1.41	4.36	6468
NM_021073	BMP5	2.02	1.83	1.78	1.51	6411
XM_002101	BMP8	2.32	10.85	1.31	0.87	6412
XM_045933	CAMKK2	2.20	1.26	1.95	1.13	6413
XM_055386	CASP1	1.40	1.76	1.89	1.45	6414

GenBank Accession-No.	Hugo-Name	Patient 1	Patient 2	Patient 3	Patient 4	SEQUENCE- ID <u>SEQ ID NO:</u>
NM_004347	CASP5	1.92	2.77	0.67	1.89	6415
NM_004166	CCL14	1.24	1.58	2.46	0.77	6463
XM_012649	SCYA7	1.24	9.78	0.85	1.82	6465
NM_001760	CCND3	1.23	2.68	1.56	1.12	6416
NM_000591	CD14	3.45	4.43	1.76	2.05	6417
XM_038773	CD164	0.84	1.91	3.26	3.15	6418
XM_048792	CD1A	3.24	3.10	1.00	1.11	6419
NM_001779	CD58	2.14	2.11	1.54	2.91	6420
XM_002948	CD80	1.69	1.16	2.25	0.69	6423
XM_027978	CFLAR	2.33	4.97	1.44	1.39	6424
NM_000760	CSF3R	1.55	1.47	1.81	1.02	6425
XM_012717	CSNK1D	1.95	3.15	1.24	1.32	6426
XM_048068	SCYD1	3.70	12.12	0.86	3.88	6466
XM_051229	CXCR4	2.33	2.10	2.15	1.60	6427
XM_039625	DUSP10	2.49	3.77	0.90	1.10	6429
XM_010177	DUSP9	2.17	5.27	1.12	1.63	6430
XM_055699	ENTPD1	1.91	3.18	0.71	0.86	6431
XM_007189	FOXO1A	1.61	3.10	1.09	1.67	6432
XM_012039	FUT4	1.55	5.07	1.88	0.93	6433
XM_040683	HPRT1	5.15	66.19	1.44	2.28	6434
NM_017526	OBRGRP	1.93	1.10	1.53	1.40	6435
XM_049516	ICAM1	1.27	1.88	2.05	1.30	6436
XM_049531	ICAM3	2.31	2.32	1.61	1.45	6437
XM_041744	IER3	4.17	7.25	1.98	2.08	6438
XM_048562	IFNAR1	2.16	4.87	1.09	2.36	6439
XM_006447	IL10RA	1.02	1.51	1.96	0.67	6440
M90391	IL-16	1.77	1.50	1.16	1.09	6441
XM_002765	IL1R2	2.84	12.75	1.03	2.75	6442
NM_000418	IL4R	3.34	6.44	2.05	2.79	6443
XM_057491	IL6	1.72	1.48	1.53	1.37	6444
NM_002184	IL6ST	2.50	9.25	1.07	1.87	6445
NM_000634	IL8RA	2.27	3.73	1.45	1.68	6446
NM_006084	ISGF3G	1.72	1.08	2.54	1.12	6447
XM_045985	ITGA2B	3.69	2.00	0.83	3.79	6448
XM_008432	ITGA3	2.11	7.62	1.08	1.06	6449
XM_028642	ITGA5	2.49	4.48	1.39	3.54	6450

GenBank Accession-No.	Hugo-Name	Patient 1	Patient 2	Patient 3	Patient 4	SEQUENCE- ID <u>SEQ ID NO:</u>
XM_036107	ITGB2	1.72	1.13	2.08	1.13	6451
XM_009064	JUNB	2.21	1.84	3.59	2.05	6452
XM_036154	LAMP2	1.79	1.68	1.62	1.41	6453
XM_042066	MAP3K1	2.06	7.67	2.91	8.93	6454
NM_001315	MAPK14	2.50	12.01	0.90	4.20	6455
NM_003684	MKNK1	2.58	17.17	1.74	1.83	6456
U68162	MPL	2.58	1.10	1.39	6.99	6457
NM_004555	NFATC3	1.40	1.70	2.80	0.75	6458
XM_006931	OLR1	1.53	5.01	1.10	3.16	6459
XM_039764	PDCD5	1.11	3.09	1.21	1.95	6460
XM_029791	PIK3C2G	0.93	1.62	0.96	1.52	6461
NM_006219	PIK3CB	1.52	0.99	0.94	1.66	6467
XM_043864	PIK3R1	1.81	4.07	1.48	1.26	6462

Please amend paragraph [0146] of the specification *as published* as follows:

[0146]

Table 3: Significantly reduced transcription activities and their relative ratio to the control sample in SIRS

GenBank Accession-No.	HUGO Name	Patient 1:	Patient 2:	Patient 3:	Patient 4:	SEQUENCE- ID <u>SEQ ID NO:</u>
BC001374	CD151	0.00	0.00	0.39	0.71	6375
XM_006454	CD3G	0.63	0.40	0.75	1.01	6378
XM_043767	CD3Z	0.43	0.00	0.82	0.77	6379
XM_056798	CD81	0.50	1.12	0.32	0.00	6380
M26315	CD8A	1.45	0.00	0.30	1.31	6381
NM_004931	CD8B1	0.40	0.90	0.50	1.19	6382

GenBank Accession-No.	HUGO Name	Patient 1:	Patient 2:	Patient 3:	Patient 4:	SEQUENCE- ID <u>SEQ ID NO:</u>
NM_001511	CXCL1	0.09	0.00	0.50	1.34	6385
XM_057158	ADCY6	1.17	0.00	0.42	1.34	6383
XM_044428	ICAM2	0.00	1.16	0.50	1.10	6386
NM_000880	IL7	0.00	1.06	0.74	0.10	6388
L34657	PECAM-1	0.68	0.39	1.13	0.64	6396
XM_044882	PTGS1	0.00	1.34	0.52	0.76	6397
XM_035842	SCYA5	0.60	0.50	0.80	0.99	6401
NM_021805	SIGIRR	0.00	0.40	0.45	0.66	6402
XM_057372	TNFRSF5	0.00	0.49	0.59	1.03	6406
NM_003809	TNFSF12	1.34	0.99	0.53	0.60	6407

Please amend paragraph [0158] of the specification *as published* as follows:

[0158] Table 5 shows that there were 24 genes found in the patient sample, which were significantly overexpressed, if compared with the control sample. Table 6 shows that there were 24 genes found in the patient sample, which were significantly underexpressed, if compared with the control sample. Those results show that the genes listed in table 5 and table 6 correlate with the occurrence of SIRS. Thus, the genes mentioned are leading genes for the diagnosis of SIRS.

Table 5: Significantly increased transcription activities and their relative ratio to the control sample in SIRS

GenBank Accession No.	HUGO Name	Patient 1:	Patient 2:	Patient 3:	SEQUENCE- ID <u>SEQ ID NO:</u>
R33626	TFAP2A	57.57	30.43	96.57	6507

GenBank Accession No.	HUGO Name	Patient 1:	Patient 2:	Patient 3:	SEQUENCE- ID SEQ ID NO:
N54839	CRSP3	47.17	29.00	63.17	6552
AA010908	LCAT	32.90	15.00	18.60	6561
R59573	TU12B1	85.50	60.50	49.00	6570
R65820	GEF	38.00	45.80	78.00	6594
N30458	NCL	26.57	20.00	17.86	6624
H86783	RINZF	43.33	17.00	31.33	6646
R11676	CDC20	30.75	52.00	55.25	6672
H79834	SLC20A2	16.56	14.33	27.44	6681
H05746	SLC12A5	70.78	20.00	17.22	6685
N21112	ARHGEF12	62.00	14.50	27.00	6693
R71085	PCANAP7	23.00	17.63	21.96	6697
R40287	NIN283	35.00	28.00	28.00	6703
H52708	PDE2A	32.78	14.11	59.22	6723
AF086381	GNPAT	18.94	19.75	25.63	6725
W57892	FN1	23.61	14.67	17.06	6753
H75516	KIN	19.23	17.15	20.00	6761
R59212	MN1	19.65	16.65	18.61	6776
H62284	CMAH	23.40	36.20	32.40	6793
W16423	GCMB	23.83	45.67	21.00	6818
N40557	U5	55.78	20.67	22.11	6826
H52695	DDC	14.80	13.70	22.30	6844
R68244	HMG14	15.81	23.19	27.56	6865
R34679	ITGB8	19.20	32.00	79.20	6874

Please amend paragraph [0159] of the specification *as published* as follows:

[0159]

Table 6: Significantly reduced transcription activities and their relative ratio to the control sample in SIRS

GenBank Accession No.	HUGO Name	Patient 1:	Patient 2:	Patient 3:	SEQUENCE- ID SEQ ID NO:
H18595	RPL10A	0.03	0.07	0.15	<u>6553</u>
N90220	DGUOK	0.04	0.07	0.12	<u>6574</u>
R19651	H19	0.09	0.07	0.19	<u>6701</u>
R52108	UBE2D2	0.13	0.07	0.02	<u>6741</u>
R83836	LYN	0.07	0.03	0.18	<u>6759</u>
H04648	CSF2RB	0.06	0.07	0.13	<u>6767</u>
H27730	PPP2R1B	0.09	0.07	0.16	<u>6788</u>
N70020	PRO2822	0.10	0.04	0.11	<u>6794</u>
N52437	CHI3L2	0.07	0.08	0.16	<u>6812</u>
W96179	GCLM	0.04	0.01	0.19	<u>6822</u>
H42506	GABARAP	0.08	0.03	0.17	<u>6842</u>
H66258	SCP2	0.10	0.05	0.21	<u>6846</u>
N38985	RAP140	0.10	0.06	0.21	<u>6896</u>
N73912	TMP21	0.09	0.07	0.08	<u>6905</u>
N51024	TEGT	0.08	0.06	0.07	<u>6909</u>
R99466	EEF1A1	0.07	0.02	0.14	<u>7008</u>
R14080	CAMLG	0.11	0.02	0.18	<u>7034</u>
W93782	XPC	0.12	0.05	0.21	<u>7036</u>

GenBank Accession No.	HUGO Name	Patient 1:	Patient 2:	Patient 3:	SEQUENCE- ID <u>SEQ ID NO:</u>
N91584	RPS6	0.06	0.05	0.12	<u>7353</u>
W52982	PIG7	0.05	0.07	0.10	<u>7412</u>
AA033725	KLF8	0.06	0.08	0.19	<u>7535</u>
N20406	SRP14	0.10	0.04	0.16	<u>7565</u>
T83104	TAF2F	0.02	0.05	0.12	<u>7630</u>
H79277	CASP8	0.12	0.06	0.13	<u>7677</u>

Please amend paragraph [00161] of the specification *as published* as follows:

[0161] In the appended sequence listing (~~SEQ. ID No:~~ SEQ ID NO: 6373 to ~~SEQ. ID No:~~ SEQ ID NO: 10540), which is part of the present invention, the gene bank accession numbers indicated in tables 5 and 6 (access via internet via <http://www.ncbi.nlm.nih.gov/>) of the individual sequences are each allocated to one sequence ID.

Please amend paragraph [0168] of the specification *as published* as follows:

[0168] Table 8 shows that 230 genes of the patient sample were found, which were significantly overexpressed (expression ratios between 13.67 and 98.33), if compared with the control sample. Table 9 [[3]] further shows that 206 genes of the patient sample were found, which were significantly underexpressed (expression ratios between 0.01 and 0.09), if compared with the control sample. Those results show that the genes listed in Tables 8 and 9 ~~table 2 and table 3~~ correlate with the occurrence of SIRS. Thus, the genes mentioned are leading genes for the diagnosis of an early sepsis.

Table 8: Expression ratio of overexpressed genes of samples of patients and controls

GenBank Gene Bank Accession No.	HUGO Name	Expression ratio of overexpressed genes compared to control	<u>SEQUENCE ID SEQ ID NO:</u>
AI086982	FLJ20623	90.13	325
AI272878	FGF20	73.48	268
AI218453	FLJ22419	48.8	294
AI473374	SPAM1	42.63	235
AI301232	PRG4	36.79	262
AI452559	FLJ13710	32	240
AI339669	FLJ21458	31	248
AI142427	CGRP-RCP	30	331
AA505969	LOC56994	26.67	486
AI333774	AGM1	26.19	251
W86875	PSEN1	25.66	903
AI591043	NR2E3	25	196
AI128812	RBM9	23.56	324
AA453019	FLJ21924	23.07	672
AI690321	KCNK15	22.71	134
AA918208	ADAM5	21.83	363
AI344681	ABCA1	21.42	259
AI654100	KIAA0610	21.04	168
AI086719	FLJ12604	20.95	326
AA453038	LOC63928	20.74	671
AI740697	SP3	20.5	114
AI332438	KIAA1033	20.17	253
AI734941	MSR1	19.93	116
AA541644	PRV1	19.51	489
AA513806	C5ORF3	19.3	485
AI381513	B4GALT7	18.81	273
AI671360	SIM1	18.55	154
AI624830	SAGE	17.54	187
AI001846	KIAA0480	17.54	358
AA504336	TRAP95	17.25	495
AI142901	IMPACT	17.15	330
AI077481	SEMA5B	17.13	327

GenBank Gene Bank Accession No.	HUGO Name	Expression ratio of overexpressed genes compared to control	SEQUENCE-ID SEQ ID NO:
H41851	TNFRSF12	17.05	1511
AI160574	FLJ23231	17	314
AI033829	KIF13B	16.59	339
AI554655	HLALS	16.59	219
AI074113	LOC51095	16.4	328
AA992716	KIAA1377	16.14	348
AI382219	SETBP1	16.08	272
AI469528	KIAA1517	15.89	232
AI090008	NFYB	15.76	349
AI203498	WRN	15.72	310
AI832179	HPGD	15.66	65
AI278521	SPRR3	15.61	265
AA909201	FLJ23129	15.12	361
AI383932	ZNF214	14.98	269
AA455096	MDM1	14.9	652
AA953859	NOL4	14.68	363
R56800	GDF1	14.67	1755
AI676097	FCER1A	14.54	151
AI380703	KIAA1268	14.51	275
AI832086	RTKN	14.51	66
AI125328	FLJ22490	14.33	317
AI056693	LOC57115	14.3	329

Please amend paragraph [00169] of the specification *as published* as follows:

[0169]

Table 9: Expression ratio of underexpressed genes of samples of patients and controls

GenBank Accession No.	Hugo Name	Expression ratio of underexpressed genes compared to control	SEQUENCE-ID SEQ ID NO:
R15296	C9ORF9	0.01	2050
AA609149	FLJ10058	0.01	375

GenBank Accession No.	Hugo Name	Expression ratio of underexpressed genes compared to control	SEQUENCE ID SEQ ID NO:
AI566451	KAI1	0.01	211
AI334246	PDCD7	0.01	250
H38679	NXPH3	0.01	1477
AI696866	KIAA1430	0.01	130
AI922915	FLJ00012	0.01	23
AI889612	KPNA6	0.01	46
AI921695	FLJ23556	0.02	26
AA410933	HRH1	0.02	764
AA705423	LOC57799	0.02	383
AI206507	RAD54B	0.02	298
AI921327	MED6	0.02	28
AI682701	VNN1	0.02	146
H82822	METAP2	0.02	1352
AI890612	MAGE1	0.02	42
AI262169	ALDOB	0.02	257
H44908	C21ORF51	0.02	1502
AI572407	FLJ22833	0.02	203
AI924869	STX4A	0.02	19
AI925556	AF140225	0.02	12
AI798388	KIAA0912	0.03	95
AI623978	SCEL	0.03	188
AI889598	MLYCD	0.03	47
AI889648	PAWR	0.03	45
AI431323	AREG	0.03	237
AA446611	CDH6	0.03	706
AI697365	P53DINP1	0.03	129
H82767	VAMP3	0.03	1353
AI688916	FLJ10933	0.03	137
AI888660	FLJ11506	0.03	51
AI890314	RAB6B	0.03	43
AI653893	LAMA5	0.03	169
R89811	HGFAC	0.03	1462
AI863022	MAGEA4	0.04	59
AA749151	XPOT	0.04	378
AI355007	ITPKB	0.04	246
AI582909	MESDC2	0.04	201
AI832016	APOL1	0.04	67
H11827	THOP1	0.04	1597
AI560205	KIAA1841	0.04	216

GenBank Accession No.	Hugo Name	Expression ratio of underexpressed genes compared to control	SEQUENCE-ID SEQ ID NO:
AA503092	UMPH1	0.04	490
AI932616	FLJ22294	0.04	5
AI799137	FLJ11274	0.04	93
AI686838	SARDH	0.04	142
AI623132	SREC	0.04	189
R96713	DKFZP434A0131	0.04	1442
AI674926	LBC	0.04	152
AI886302	HRI	0.04	53
AI434650	MGC2560	0.04	238
AI631380	GNG4	0.04	180
AA508868	ORC6L	0.04	491
AI620374	HP1-BP74	0.04	190
AI679115	KIAA1353	0.04	148
AA652703	MRPL49	0.04	386
AI355775	CDK3	0.04	245

Please amend paragraph [00186] of the specification *as published* as follows:

[0186] K4 in FIG. 1 and in FIG. 2 is the acute phase protein transthyretin (TTR; P02766, ~~SEQ-~~ SEQ ID NO: 6241, ~~SEQ-ID~~ SEQ ID NO: 6242) and K5 and K6 are the vitamin D-binding protein (DBP; P02774, ~~SEQ-ID~~ SEQ ID NO: 1554, ~~SEQ-ID~~ SEQ ID NO: 1555).

Please amend paragraph [00190] of the specification *as published* as follows:

[0190] A comparing analysis shows (FIG. 1, FIG. 2) that the acute phase protein transthyretin (TTR; P02766, ~~SEQ-ID~~ SEQ ID NO: 6241, ~~SEQ-ID~~ SEQ ID NO: 6242), as well as the vitamin D-binding protein (DBP; P02774, ~~SEQ-ID~~ SEQ ID NO: 1554, ~~SEQ-ID~~ SEQ ID NO: 1555) are less expressed by the sepsis patient, if compared with the control patient.

Please amend paragraph [0203] of the specification *as published* as follows:

[0203] Table 12 shows that 41 genes of the patient sample were found, which were significantly overexpressed, if compared with the control sample. Table 13 shows that 89 genes of the patient sample were found, which were significantly underexpressed, if compared with the control sample. Those results show that the genes listed in table 12 and table 13 correlate with the occurrence of a severe sepsis. Furthermore, these results correlate with the clinical classification according to [4] as well as patients' PCT-concentrations, that are typical for the occurrence of a severe sepsis [23]. Thus, the gene activities of the genes mentioned are labels for the diagnosis of a severe sepsis.

Table 12: Expression ratio of overexpressed genes of samples of patients and controls

GenBank Accession No.	HUGO Name	Expression ratio of overexpressed genes compared to control	SEQUENCE- ID <u>SEQ ID NO:</u>
XM_086400	S100A8	4.4	<u>6243</u>
XM_001682	S100A12	3.03	<u>6244</u>
NM_002619	PF4	2.21	<u>6245</u>
NM_002704	PPBP	1.66	<u>6246</u>
NM_001101	ACTB	1.65	<u>6247</u>
NM_001013	RPS9	1.61	<u>6248</u>
XM_057445	SELP	1.61	<u>6249</u>
BC018761	IGKC	1.53	<u>6250</u>
XM_030906	TGFB1	1.51	<u>6251</u>
NM_001760	CCND3	1.48	<u>6252</u>
XM_035922	IL11	1.28	<u>6253</u>
XM_039625	DUSP10	1.17	<u>6254</u>
XM_002762	TNFAIP6	1.17	<u>6255</u>
XM_015396	ALOX5AP	1.15	<u>6256</u>
NM_003823	TNFRSF6B	1.15	<u>6257</u>
XM_029300	DPP4	1.15	<u>6258</u>

GenBank Accession No.	HUGO Name	Expression ratio of overexpressed genes compared to control	SEQUENCE- ID <u>SEQ ID NO:</u>
NM_001562	IL18	1.14	<u>6259</u>
NM_005037	PPARG	1.11	<u>6260</u>
M90746	FCGR3B	1.07	<u>6261</u>
NM_001315	MAPK14	0.99	<u>6262</u>
BC001506	CD59	0.88	<u>6263</u>
XM_042018	BSG	0.88	<u>6264</u>
XM_010177	DUSP9	0.87	<u>6265</u>
BC013992	MAPK3	0.84	<u>6266</u>
NM_001560	IL13RA1	0.82	<u>6267</u>
NM_004555	NFATC3	0.74	<u>6268</u>
NM_001154	ANXA5	0.73	<u>6269</u>
NM_001310	CREBL2	0.7	<u>6270</u>
XM_036107	ITGB2	0.65	<u>6271</u>
XM_009064	JUNB	0.65	<u>6272</u>
NM_001774	CD37	0.62	<u>6273</u>
XM_049849	TNFRSF14	0.6	<u>6274</u>
NM_003327	TNFRSF4	0.57	<u>6275</u>
BC001374	CD151	0.56	<u>6276</u>
XM_051958	ALOX5	0.56	<u>6277</u>
NM_021805	SIGIRR	0.5	<u>6278</u>
NM_017526	HSOBRGR	0.48	<u>6279</u>
XM_011780	DAPK1	0.46	<u>6280</u>
NM_006017	PROML1	0.44	<u>6281</u>
D49410	IL3RA	0.43	<u>6372</u>
XM_027885	RPL13A	0.33	<u>6282</u>

Please amend paragraph [0204] of the specification *as published* as follows:

[0204]

Table 13: Expression ratio of underexpressed genes of samples of patients and controls

GenBank Accession No.	HUGO Name	Expression ratio of underexpressed genes compared to control	SEQUENCE- ID <u>SEQ ID NO:</u>
NM_007289	MME	-2.11	6283
XM_008411	SCYA13	-2.06	6284
XM_055188	ENG	-2.01	6285
NM_021073	BMP5	-1.99	6286
XM_007417	TGFB3	-1.93	6287
NM_001495	GFRA2	-1.88	6288
XM_009475	AHCY	-1.86	6289
XM_006738	CD36L1	-1.86	6290
NM_001772	CD33	-1.86	6291
NM_057158	DUSP4	-1.83	6292
XM_058179	CD244	-1.77	6293
NM_001770	CD19	-1.75	6294
NM_004931	CD8B1	-1.73	6295
XM_006454	CD3G	-1.71	6296
XM_041847	TNF	-1.65	6297
NM_145319	MAP3K6	-1.62	6298
XM_045985	ITGA2B	-1.61	6299
XM_055756	TIMP1	-1.61	6300
NM_004740	TIAF1	-1.61	6301
XM_008432	ITGA3	-1.57	6302
XM_034770	PAFAH1B1	-1.56	6303
NM_014326	DAPK2	-1.55	6304
XM_043864	PIK3R1	-1.49	6305
U54994	CCR5	-1.49	6306
NM_004089	DSIP1	-1.49	6307
XM_037260	F2R	-1.45	6308
NM_172217	IL16	-1.45	6309
AF244129	LY9	-1.45	6310
NM_003775	EDG6	-1.43	6311
NM_001781	CD69	-1.41	6312
NM_019846	CCL28	-1.39	6313
NM_001511	CXCL1	-1.38	6314
NM_006505	PVR	-1.33	6315
NM_000075	CDK4	-1.33	6316
XM_042066	MAP3K1	-1.32	6317
NM_003242	TGFBR2	-1.31	6318
NM_003874	CD84	-1.31	6319

GenBank Accession No.	HUGO Name	Expression ratio of underexpressed genes compared to control	SEQUENCE- ID <u>SEQ ID NO:</u>
XM_033972	ATF6	-1.3	6320
XM_001840	PLA2G2A	-1.3	6321
NM_018310	BRF2	-1.29	6322
AF212365	IL17BR	-1.25	6323
XM_056798	CD81	-1.25	6324
NM_000061	BTK	-1.24	6325
XM_001472	JUN	-1.23	6326
XM_007258	TNFAIP2	-1.23	6327
XM_048555	IFNAR2	-1.23	6328
XM_041060	FOS	-1.23	6329
XM_056556	TNFSF7	-1.23	6330
XM_016747	LTBP1	-1.22	6331
XM_006953	TNFRSF7	-1.21	6332
NM_015927	TGFB1I1	-1.19	6333
XM_010807	INHBB	-1.16	6334
NM_002184	IL6ST	-1.14	6335
XM_008570	VAMP2	-1.13	6336
NM_006856	ATF7	-1.1	6337
NM_000674	ADORA1	-1.09	6338
NM_000173	GP1BA	-1.08	6339
XM_048068	SCYD1	-1.07	6340
NM_022162	CARD15	-1.07	6341
NM_001199	BMP1	-1.02	6342
NM_000960	PTGIR	-1.01	6343
XM_012039	FUT4	-0.99	6344
XM_034166	NOS2A	-0.99	6345
NM_003188	MAP3K7	-0.98	6346
NM_006609	MAP3K2	-0.98	6347
XM_027358	PCMT1	-0.95	6348
XM_007189	FOXO1A	-0.93	6349
XM_030523	MAP3K8	-0.92	6350
XM_002923	CCR2	-0.88	6351
XM_054837	TNFRSF1B	-0.87	6352
NM_000634	IL8RA	-0.87	6353
NM_004590	CCL16	-0.86	6354
XM_012717	CSNK1D	-0.86	6355
XM_012649	SCYA7	-0.84	6356

GenBank Accession No.	HUGO Name	Expression ratio of underexpressed genes compared to control	SEQUENCE- ID <u>SEQ ID NO:</u>
XM_008679	TP53	-0.84	6357
XM_030509	PTGIS	-0.83	6358
XM_039086	CDW52	-0.82	6359
XM_027978	CFLAR	-0.81	6360
NM_005343	HRAS	-0.79	6361
XM_043574	DAP3	-0.78	6362
NM_002188	IL13	-0.77	6363
XM_055699	ENTPD1	-0.72	6364
NM_000565	IL6RA	-0.67	6365
NM_002211	ITGB1	-0.65	6366
XM_049864	CSF3	-0.63	6367
XM_045933	CAMKK2	-0.63	6368
NM_033357	CASP8	-0.55	6369
XM_008704	DNAM-1	-0.52	6370
NM_030751	TCF8	-0.5	6371

Please amend paragraph [0206] of the specification *as published* as follows:

[0206] In the appended sequence listing, which is part of the present invention, the gene bank accession numbers (access via internet via <http://www.ncbi.nlm.nih.gov/>) indicated in tables 12 and 13 of the individual sequences are each allocated to one sequence ID. (~~SEQ. ID No.:~~ SEQ ID NO: 6243 to ~~SEQ. ID No.:~~ SEQ ID NO: 6372). The following sequence listing is part of the present invention.